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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/584,874
Filing Date: June 07, 2007
Appellant(s): BENATTI ET AL.

James J. Napoli
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed March 25, 2010 appealing from the Office action mailed October 1, 2009.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

The following is a listing of the evidence (e.g., patents, publications, Official Notice, and admitted prior art) relied upon in the rejection of claims under appeal.

US-5,464,825 11-1995 Anderson et al (as cited in IDS 6/8/07).

McMurry, Organic Chemistry 4th Edition, 1996, page 825 (first cited 6/10/08).

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Appellant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 15, 17-18 and 23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anderson et al. (US 5,464,825; cited with IDS 6/8/07) and McMurry (Organic Chemistry 4th edition 1996, page 825; first cited with office action 6/10/08).

Anderson et al teach methods for increasing glutathione (GSH) levels or levels of glutathione equivalents (column 3 lines 22-23). Anderson specifically recites N-acyl glutathiones as a type of glutathione derivative (column 3 line 24). Anderson teaches that the acyl group can contain 1 to 9 carbon atoms and is preferably 1 to 4 carbon atoms, for example propyl (column 3

lines 33-37). Anderson et al teach that acylated esters are de-esterified in the cell (column 3 line 29,67).

Anderson et al teach that elevated GSH levels are desired in the treatment of viral infections (column 3 lines 11-18).

Anderson et al specifically teach compounds identified as N-acetyl GSH monoesters (column 4 lines 10-30). Anderson et al specifically teach that the R1 is preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). Anderson et al teach that the compounds are hydrolyzed (column 4 line 21) to form N-acyl GSH which is the de-esterified compound. Anderson et al teach pharmaceuticals of such compounds (column 4 lines 30-32). Anderson et al do not expressly show the reaction scheme of the hydrolysis reaction. McMurry (bottom of page 825) teaches that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson et al (column 4, line 21) includes a carboxylic acid not an ester.

Neither of the references expressly teaches the compound of the instant invention.

Anderson et al specifically teach compounds identified as N-acetyl GSH monoesters (column 4 lines line 10-30). Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48). One would recognize that R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. For example R1 can be methyl, ethyl, or propyl. When R1 is propyl and the compound is de-esterified (column 3, lines 29, 67) or hydrolyzed (column 4, line 21) as described by Anderson et al the resulting product is a carboxylic acid that is identical to the

elected species of claim 15 of the instant invention where R is H (the elected species). Thus the limitations of claims 15 are met.

In other words, the disclosure of 'N-acyl GSH' (column 4, line 21) includes various compounds that have been hydrolyzed. Since Anderson et al teach such compounds as pharmaceuticals (column 4, lines 30-32), teach carriers (column 5, lines 23-30) and teach applications for treatment of viral infections (column 2, lines 11-18), the limitations of claims 17-18 and 23 are met.

It has been recently held that "obvious to try" may be an appropriate test under 103 KSR v. Teleflex, 550 U.S. ___, 82 USPQ2d 1385, 1389 (2007). The Supreme Court stated in *KSR*

> When there is motivation
>
> > "to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to anticipated success, it is likely the product not of innovation but of ordinary skill and common sense. In that instance the fact that a combination was obvious to try might show that it was obvious under § 103." *KSR Int'l Co. v. Teleflex Inc.*, 127 S. Ct. 1727, ___, 82 USPQ2d 1385, 1397 (2007).

In the instant case, the claims would have been obvious because 'a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product nor of innovation but of ordinary skill and common sense'. In particular, Anderson et al teach a finite number of compounds to be used (column 4, lines 10-30). Further, Anderson et al specifically teach R1 values and teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48). One would recognize that the compound with R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. Further, such compounds are described as being de-esterified and hydrolyzed. From the teachings of the references, it is

apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

10) Response to Argument

Appellants Arguments – 103 rejection

Appellants recite case law (pages 9-14), recite excerpts of the rejection and references (pages 14-15, 17) and argue (pages 15-16) that '825 teaches use in cells.

Appellants argue (pages 15-16 and 18-19) that the claimed compounds require a carboxyl group, butanoyl group and hydrogen at specific locations and that the there are differences in structure.

Appellants argue (pages 15-16,19-21,26-28) that the '825 patent teaches the necessity of the monoester for transport and teach that intact GSH is not delivered into the cell and that the reference leads one away from the presently claimed compounds.

Appellants argue (pages 20-21) that modifications in structure can change pharmacokinetics and that it cannot be predicted that changing the ester moiety of the '825 patent to a carboxylic acid would provide a useful drug and that the examples of '825 show that GSH only had a slight effect in the kidneys.

Appellants argue (pages 21-22) that it could not have been predicted that certain compounds would reach the cells.

Appellants argue (pages 22-23, 28) that the instant invention is unexpected and in contrast to the teachings of '825 since the claims do not require an esterified glycine residue.

Appellants argue (pages 22 and 24) that certain compounds are of low activity or are toxic and the results could not have been predicted.

Appellants argue (page 22) that there is not incentive to perform a hydrolysis.

Appellants argue (page 23) that a teaching or suggestion must be found in the prior art and the reasonable expectation of success must be found in the prior art.

Appellants argue (page 23) that the modification suggested by the examiner would not provide a reasonable expectation of increasing intracellular GSH levels.

Appellants argue (pages 23-24 and 31) that there is no reason to modify the reference and that the GSH does not work or only performed marginally so there is no expectation of success.

Appellants argue (pages 25 and 30-32) that the instant compounds are different from those of '825 and the compounds have been compared to other compounds.

Appellants argue (pages 26-27) that although '825 refers to pharmaceutical salts there is a misinterpretation about the compounds.

Appellants argue (page 27) that the art suggests the use of mono-ester derivative.

Appellants argue (page 28) that the references never considered using an N-acyl GSH compound.

Appellants argue (page 29) that they are giving the '825 patent the benefit of any doubt regarding efficacy of the disclosed compounds.

Appellants argue (pages 32-33) that the instant specification states that GSH-C4 has the best effects.

Response to Arguments

Although Appellants recite case law (pages 9-14), recite excerpts of the rejection and references (pages 14-15 and 17) and argue (page 15-16) that '825 teach use in cells, it is first noted that Appellants do not directly argue specifics about the case law in relation to the instant claims. As such, the case law citations appear to be background information and there are no specifics to address. With respect to use in cells, it is noted that claim 15 is drawn to a compound with no specific use recited in the claims. It is noted that the features upon which Appellants rely (i.e., use in cells) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Although Appellants argue (pages 15-16 and 18-19) that the claimed compounds require a carboxyl group, butanoyl group and hydrogen at specific locations and that the there are differences in structure, it is noted that the instant rejection is not a 102 rejection, but is a 103 rejection. As such, the claims are not necessarily anticipated. With regards to the specific elected compound, the prior art obviates the instant structure. Although Appellants argue that the invention has a carboxylic residue while the art teaches an ester (positions 2 and 2' of Appellants' nomenclature), Anderson et al teach that the compounds are hydrolyzed (column 4, line 21) to form N-acryl GSH, which is the de-esterified compound. In other words, the disclosure of 'N-acyl GSH' (column 4, line 21) includes various compounds that have been hydrolyzed. McMurry (bottom of page 825) teach that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid

product. In particular the N-acyl GSH recited by Anderson (column 4, line 21) includes a carboxylic acid not an ester. Thus Anderson's disclosure of 'N-acyl GSH' (column 4, line 21) and teachings of de-esterification (column 3, lines 29 and 67) results in compounds which meet the claim limitations with regards to a carboxylic residue. Although Appellants argue that the invention has a propyl group while the art teach numerous residues (position 3 and 3'), Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48). One would recognize that R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. For example R1 can be methyl, ethyl, or propyl. In the instant case, Anderson et al expressly suggest (i.e. 'preferably 1 to 3 carbon atoms', see column 4, lines 44-48) propyl. Although Appellants argue that the invention has a hydrogen or acetyl while the art teach hydrogen (position 1 and 1'), such argument supports the instant rejection. Claim 1 recites that R can be H. Since the art teach that R is H the claim limitation is met.

Although Appellants argue (pages 15-16,19-21 and 26-28) that the '825 patent teaches the necessity of the monoester for transport and teach that intact GSH is not delivered into the cell and that the reference leads one away from the presently claimed compounds, it is noted that the instant claims are drawn to compounds. The claims do not recite any information with respect to transport. Furthermore, the instant claims are not drawn to GSH. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). As discussed above, the structural limitations of the claims are obviated by the prior art. Further, if the prior art structure is capable of performing the intended use, then it meets the claim. Section 2123 II

of the MPEP expressly states that alternative embodiments are prior art. In column 4, line 21 Anderson et al expressly teach N-acyl GSH and then goes on to state that pharmaceutically acceptable salts of the above compounds, which include N-acyl GSH, are within the scope of the present invention (column 4, lines 30-32). Thus Anderson et al expressly teach that the N-acyl GSH compounds and salts thereof are within the scope of the invention. Further, section 2144.09 of the MPEP (last paragraph) states:

> However, a claimed compound may be obvious because it was suggested by, or structurally similar to, a prior art compound even though a particular benefit of the claimed compound asserted by patentee is not expressly disclosed in the prior art. It is the differences in fact in their respective properties which are determinative of nonobviousness. If the prior art compound does in fact possess a particular benefit, even though the benefit is not recognized in the prior art, applicant's recognition of the benefit is not in itself sufficient to distinguish the claimed compound from the prior art. In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).

In the instant case, the prior art suggests that the monoester can be converted via hydrolysis to the carboxylic acid (column, 4 lines 18-24). Further, Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48). Further, even if one started with a mono-ester compound, the reaction scheme, as shown in column 4, clearly shows that an N-acyl GSH compound would be formed via hydrolysis. Further, Anderson et al teach a goal of increasing GSH levels or glutathione equivalents (N-acyl glutathiones) (abstract). If the prior art only considered the ester as important the prior art would not have shown the hydrolysis reaction to make the N-acyl GSH (see column 4).

Although Appellants argue (pages 20-21) that modifications in structure can change pharmacokinetics and that it cannot be predicted that changing the ester moiety of the '825 patent to a carboxylic acid would provide a useful drug and that the examples of '825 show that

GSH only had a slight effect in the kidneys, it is first noted that claim 15 is not drawn to a drug nor is claim 15 drawn to GSH. Further, the methods are not drawn to methods of changing pharmacokinetics. Claim 15 is simply drawn to compounds. The prior art obviates claim 15. With regards to predictability, in column 4, line 21 Anderson et al teach N-acyl GSH and then goes on to state that pharmaceutically acceptable salts of the above compounds, which include N-acyl GSH, are within the scope of the present invention (column 4, lines 30-32). Thus Anderson et al expressly teach that the N-acyl GSH compounds and salts thereof are within the scope of the invention. Whether or not a change in structure can result in changes does not discredit the teachings of the prior art. Although the teachings of Anderson et al may suggest that certain compounds may be more effective than others, section 2123 of the MPEP states:

> Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

The schematic shown in column 4 of Anderson, expressly teaches that N-acyl GSH is converted via deacylation to GSH. Thus N-acyl GSH is the immediate precursor to GSH. If the level of the immediate precursor (i.e. N-acyl GSH) is increased, there is a reasonable basis that GSH levels will increase.

Although Appellants argue (pages 21-22) that it could not have been predicted that certain compounds would reach the cells, it is noted that claim 15 is drawn to a compound with no specific use recited in the claims. It is noted that the features upon which Appellants rely (i.e., use in cells) are not recited in the rejected claim(s). Although the claims are interpreted in

light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

Although Appellants argue (pages 22-23,28) that the instant invention is unexpected and in contrast to the teachings of '825 since the claims do not require an esterified glycine residue, Anderson et al teach that the compounds are hydrolyzed (column, 4 line 21) to form N-acyl GSH which is the de-esterified compound. In other words, the disclosure of 'N-acyl GSH' (column 4, line 21) includes various compounds that have been hydrolyzed. McMurry (bottom of page 825) teach that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson et al (column 4, line 21) includes a carboxylic acid not an ester. In column 4, line 21, Anderson et al teach N-acyl GSH and then goes on to state that pharmaceutically acceptable salts of the above compounds, which include N-acyl GSH, are within the scope of the present invention (column 4, lines 30-32). Thus Anderson et al expressly teach that the N-acyl GSH compounds and salts thereof are within the scope of the invention.

Although Appellants argue (page 22-24) that certain compounds are of low activity or are toxic and the results could not have been predicted, it is noted that page 6, lines 17-21 and pages 12, lines 4-6 merely imply that GSH-C4 was the best compound and page 11, lines 27-28 imply that C8 and C12 derivatives were not optimal. Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48). Since Anderson expressly suggest (and prefer) 1 to 3 carbons one would expect such compounds to have more desirable properties that C12 derivatives for example. More simply, GSH is a rather small molecule and the addition of 12 carbons would essentially double the length of the

molecule and a large portion of the molecule would not even resemble the parent molecule. However, the 1 to 3 carbon preferences as taught by Anderson et al result in relatively minor structural changes. Section 716.02 of the MPEP states:

> Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (differences in sedative and anticholinergic effects between prior art and claimed antidepressants were not unexpected). In In re Waymouth, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974), the court held that unexpected results for a claimed range as compared with the range disclosed in the prior art had been shown by a demonstration of "a marked improvement, over the results achieved under other ratios, as to be classified as a difference in kind, rather than one of degree." Compare In re Wagner, 371 F.2d 877, 884, 152 USPQ 552, 560 (CCPA 1967) (differences in properties cannot be disregarded on the ground they are differences in degree rather than in kind); Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) ("we generally consider a discussion of results in terms of differences in degree' as compared to differences in kind' . . . to have very little meaning in a relevant legal sense").

In the instant case, when testing a group of compounds, one would expect that the compounds would not behave identically. If one were to expect all compounds to behave identically there would be no tests performed. Anderson et al teach that certain derivatives are known to show some toxic effects (column 2, lines 38-39). Further, Anderson et al expressly teach that the alkyl chain preferably contain 1 to 3 carbons (column 4, lines 44-47) which includes propyl. Since Anderson et al expressly teach that propyl is preferred, one would expect such compound to have more desirable properties. It is noted that it appears that appellants may be attempting to show a criticality (compare MPEP 716.02(d) II) of the carbon chain length. However, Anderson et al expressly teach that the alkyl chain preferably contain 1 to 3 carbons (column 4, lines 44-47). Further, appellants' specification state that GSH-C4 showed the best effects (page 12, lines 8-15). A showing of 'best effects' does not show that the range is 'critical'. In the instant case,

when testing a group of compounds, one would expect that the compounds would not behave identically.

Although Appellants argue (page 22) that there is not incentive to perform a hydrolysis, such assertion is not supported by the prior art. Anderson et al teach that the compounds are hydrolyzed (column 4, line 21) to form N-acyl GSH which is the de-esterified compound. In other words, the disclosure of 'N-acyl GSH' (column 4, line 21) includes various compounds that have been hydrolyzed. McMurry (bottom of page 825) teaches that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson (column 4, line 21) includes a carboxylic acid not an ester. Thus Anderson et al's teaching of 'N-acyl GSH' (column 4, line 21) and teachings of de-esterification (column 3, lines 29,67) results in compounds which meet the claim limitations with regards to a carboxylic residue. In the instant case, one would be motivated by the express teachings of the prior art (see for example the schematic in column 4 of Anderson et al).

Although Appellants argue (page 23) that a teaching or suggestion must be found in the prior art and the reasonable expectation of success must be found in the prior art, the prior art does provide teachings and an expectation of success. Anderson et al teach that the compounds are hydrolyzed (column 4, line 21) to form N-acyl GSH which is the de-esterified compound. In other words, the disclosure of 'N-acyl GSH' (column 4, line 21) includes various compounds that have been hydrolyzed. McMurry (bottom of page 825) teaches that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson et al (column 4, line

21) includes a carboxylic acid not an ester. Thus Anderson et al's teaching of 'N-acyl GSH' (column 4, line 21) and teachings of de-esterification (column 3, lines 29,67) results in compounds which meet the claim limitations with regards to a carboxylic residue. Although Appellants argue that the invention has a propyl group while the art teach numerous residues (position 3 and 3'), Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4 line 44-48). One would recognize that R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. For example R1 can be methyl, ethyl, or propyl. In column 4, line 21 Anderson et al teach N-acyl GSH and then go on to state that pharmaceutically acceptable salts of the above compounds, which include N-acyl GSH, are within the scope of the present invention (column 4, lines 30-32). Thus Anderson et al expressly teach that the N-acyl GSH compounds and salts thereof are within the scope of the invention. Further, with regards to predictability, Anderson et al expressly set forth the reactions to result in N-acyl GSH compounds (see column 4). Further, with respect to motivation Anderson et al teach methods for increasing glutathione (GSH) levels or levels of glutathione equivalents (column 3, lines 22-23). Anderson et al teach that elevated GSH levels are desired in the treatment of viral infections (column 3, lines 11-18).

Although Appellants argue (page 23) that the modification suggested by the examiner would not provide a reasonable expectation of increasing intracellular GSH levels, it is noted that the features upon which Appellants rely (i.e., increasing GSH levels) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Further, the schematic shown in column 4 of Anderson,

expressly teach that N-acyl GSH is converted via deacylation to GSH. Thus N-acyl GSH is the immediate precursor to GSH. If the level of the immediate precursor (i.e. N-acyl GSH) is increased, there is a reasonable basis that GSH levels will increase.

Although Appellants argue (page 23-24 and 31) that there is no reason to modify the reference and that the GSH does not work or only performed marginally so there is no expectation of success, the motivation to modify expressly comes from the prior art reference (i.e. Anderson et al). Since Anderson et al teach a genus of compounds (see column 4) one would recognize that Anderson et al is not limited to a single compound. Further, such compounds as described by Anderson et al have an intended use (see abstract). In column 4, line 21 Anderson et al teach N-acyl GSH and then go on to state that pharmaceutically acceptable salts of the above compounds, which include N-acyl GSH, are within the scope of the present invention (column 4 lines 30-32). Thus Anderson et al expressly teach that the N-acyl GSH compounds and salts thereof are within the scope of the invention. With regard to GSH, it is noted that the instant claims are not drawn to GSH. Further, Anderson et al teach (column 2 lines 40-50) that GSH alone may lead to increases in GSH levels.

Although Appellants argue (pages 25 and 30-32) that the instant compounds are different from those of '825 and the compounds have been compared to other compounds, it is noted that the instant rejection is not a 102 rejection, but is a 103 rejection. As such, the claims are not necessarily anticipated. With regards to the specific elected compound, the prior art obviate the instant structure. Although Appellants argue that the invention has a carboxylic residue while the art teaches an ester (positions 2 and 2' of Appellants' nomenclature), Anderson et al teach that the compounds are hydrolyzed (column 4, line 21) to form N-acyl GSH which is the de-

esterified compound. In other words, the disclosure of 'N-acyl GSH' (column 4, line 21) includes various compounds that have been hydrolyzed. McMurry (bottom of page 825) teaches that esters are hydrolyzed to form carboxylic acids. McMurry is cited to show that de-esterification (by hydrolysis) results in a carboxylic acid product. In particular the N-acyl GSH recited by Anderson et al (column 4, line 21) includes a carboxylic acid not an ester. Thus Anderson et al disclosure of 'N-acyl GSH' (column 4, line 21) and teachings of de-esterification (column 3, line 29 and 67) results in compounds which meet the claim limitations with regards to a carboxylic residue. Although Appellants argue that the invention has a propyl group while the art teach numerous residues (position 3 and 3'), Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, line 44-48). One would recognize that R1 being hydrocarbon with preferably 1 to 3 carbons represents a finite number of possible compounds. For example R1 can be methyl, ethyl, or propyl. In the instant case, Anderson et al expressly suggest (i.e. 'preferably 1 to 3 carbon atoms' column 4 lines 44-48) propyl. Although Appellants argue that the invention has a hydrogen or acetyl while the art teach hydrogen (position 1 and 1'), such argument supports the instant rejection. Claim 1 recites that R can be H. Since the art teaches that R is H, the claim limitation is met. With regards to the comparisons to other compounds, such comparisons do not show an unexpected result. Section 716.02(b) of the MPEP states that the burden is on the appellants to establish results are unexpected and significant.

Although Appellants argue (pages 26-27) that although '825 refers to pharmaceutical salts, there is a misinterpretation about the compounds; '825 patent expressly recites (column 4, lines 30-32) 'salts of the above compounds are within the scope of the present invention'. One

of the compounds listed above such phrase is N-acyl GSH. 'Above compounds' means 'above compounds'. If the intent was to only refer to a subset of compounds alternate language would have been used (for example 'above compounds except for xxx').

Although Appellants argue (page 27) that the art suggests the use of mono-ester derivative, section 2123 of the MPEP states:

> Disclosed examples and preferred embodiments do not constitute a teaching away from a broader disclosure or nonpreferred embodiments. In re Susi, 440 F.2d 442, 169 USPQ 423 (CCPA 1971). "A known or obvious composition does not become patentable simply because it has been described as somewhat inferior to some other product for the same use." In re Gurley, 27 F.3d 551, 554, 31 USPQ2d 1130, 1132 (Fed. Cir. 1994).

In the instant case, in column 4, line 21 Anderson et al teach N-acyl GSH and then goes on to state that pharmaceutically acceptable salts of the above compounds, which include N-acyl GSH, are within the scope of the present invention (column 4 lines 30-32). Thus Anderson et al expressly teach that the N-acyl GSH compounds and salts thereof are within the scope of the invention. Further, even is one started with a mono-ester compound the reaction scheme as shown in column 4 clearly shows that an N-acyl GSH compound would be formed via hydrolysis.

Although Appellants argue (page 28) that the references never considered using an N-acyl GSH compound, it is noted that the claims are not drawn to methods of use. Section 2144.09 of the MPEP (last paragraph) states:

> However, a claimed compound may be obvious because it was suggested by, or structurally similar to, a prior art compound even though a particular benefit of the claimed compound asserted by patentee is not expressly disclosed in the prior art. It is the differences in fact in their respective properties which are determinative of nonobviousness. If the prior art compound does in fact possess a particular benefit, even though the benefit is not recognized in the prior art, applicant's recognition of the benefit

> is not in itself sufficient to distinguish the claimed compound from the prior art. In re Dillon, 919 F.2d 688, 16 USPQ2d 1897 (Fed. Cir. 1991).

In the instant case, the prior art suggests that the monoester can be converted via hydrolysis to the carboxylic acid (column 4, lines 18-24). Further, Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48).

Although Appellants argue (page 29) that they are giving the '825 patent the benefit of any doubt regarding efficacy of the disclosed compounds, such arguments supports predictability and hence support the instant rejections. Further, it is noted that claim 15 is drawn to compounds with no functional properties recited.

Although Appellants argue (page 32-33) that the instant specification states that GSH-C4 has the best effects, Section 716.02 of the MPEP states:

> Any differences between the claimed invention and the prior art may be expected to result in some differences in properties. The issue is whether the properties differ to such an extent that the difference is really unexpected. In re Merck & Co., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986) (differences in sedative and anticholinergic effects between prior art and claimed antidepressants were not unexpected). In In re Waymouth, 499 F.2d 1273, 1276, 182 USPQ 290, 293 (CCPA 1974), the court held that unexpected results for a claimed range as compared with the range disclosed in the prior art had been shown by a demonstration of "a marked improvement, over the results achieved under other ratios, as to be classified as a difference in kind, rather than one of degree." Compare In re Wagner, 371 F.2d 877, 884, 152 USPQ 552, 560 (CCPA 1967) (differences in properties cannot be disregarded on the ground they are differences in degree rather than in kind); Ex parte Gelles, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992) ("we generally consider a discussion of results in terms of differences in degree' as compared to differences in kind' . . . to have very little meaning in a relevant legal sense").

In the instant case, when testing a group of compounds, one would expect that the compounds would not behave identically. If one were to expect all compounds to behave identically there would be no tests performed. Anderson et al teach that certain derivatives are known to show

some toxic effects (column 2, lines 38-39). Further, Anderson et al expressly teach that the alkyl chain preferably contain 1 to 3 carbons (column 4, lines 44-47) which includes propyl. Since Anderson et al expressly teach that propyl is preferred, one would expect such compound to have more desirable properties.

In summary, Anderson et al teach a goal of increasing GSH levels or glutathione equivalents (N-acyl glutathiones) (abstract). Anderson et al specifically teach compounds identified as N-acetyl GSH monoesters (column 4, lines 10-30). Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48). Anderson et al teach hydrolysis of the esters to form N-acyl GSH (column 4, line 21). Thus, Anderson et al motivate compounds (based on the recited uses, preferences, and reactions schemes) that read on the instant claims. Section 716.02(b) of the MPEP states that the burden is on the applicant to establish results are unexpected and significant. Anderson et al specifically teach that the R1 is hydrocarbon with preferably 1 to 3 carbons and can be propyl (column 4, lines 44-48).

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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